Baghlaf K, Muirhead V, Moynihan P, Weston-Price S, Pine C.

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Free sugars consumption around bedtime and dental caries in children. A Systematic Review.

Khlood Baghlaf,[1], Vanessa Muirhead ,[2], Paula Moynihan ,[3]

Sally Weston-Price,[4] and Cynthia Pine,[5]

[1] PhD Student, Institute of Dentistry, Queen Mary University of London, UK, and Lecturer, King Abdulaziz University, Faculty of Dentistry, Pediatric Dentistry Department, Jeddah, Kingdom of Saudi Arabia.

[2] Clinical Senior Lecturer/Honorary Consultant in Dental Public Health, Institute of Dentistry, Queen Mary University of London, UK
Email: v.muirhead@qmul.ac.uk

[3] Professor of Nutrition and Oral Health, Centre for Oral Health Research, School of Dental Sciences, Newcastle University, Newcastle, UK.
Email: paula.moynihan@newcastle.ac.uk

[4] National Institute of Health Research Academic Clinical Fellow in Dental Public Health, Institute of Dentistry, Queen Mary University of London, UK.
Email: s.weston-price@qmul.ac.uk

[5] Professor of Dental Public Health, Institute of Dentistry, School of Medicine and Dentistry, Queen Mary University of London, UK.
Email: c.m.pine@qmul.ac.uk.

Corresponding author: Khlood Baghlaf
Contact information: Institute of Dentistry, Queen Mary University of London, UK, Royal London Dental Hospital, Turner Street, London, UK E1 2AD
Email: k.k.h.baghlaf@qmul.ac.uk
Telephone number: +44 (0) 207 882 7526

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Abstract

This systematic review aimed to assess the association between food and drink consumption and specifically consuming food and drinks containing free sugars around bedtime and the risk of dental caries in children. Five electronic databases were searched (PubMed, Ovid Medline, EMBASE, Web of science and Scopus) to identify studies that investigated any relationship between food and drink around bedtime and dental caries in three to 16-year-old children. The Agency for Healthcare Research and Quality (AHRQ) domain guidelines were used to assess the quality of the individual studies, while GRADE guidelines assessed the quality of studies based on the body of evidence.

From 1270 retrieved titles, 777 remained after removing duplicates. Of these 72 were reviewed in full. Eighteen papers fulfilled the inclusion criteria and were included in the analysis: 13-cross-sectional, four cohort, and one case-control study. Studies were categorized into three age groups: 3-5 year old children, 6-11 year old children and 12-16 year old children.

Based on the AHRQ criteria, six of the 18 studies were rated as providing good quality evidence; eight were rated as fair and four were categorised as of poor quality. It was not possible to conduct a meta-analysis because of the considerable variations in the type of bedtime exposure and outcome measures. The studies showed a consistent positive association across the three age groups with all seven studies on preschool children reporting significant positive associations. However, the quality of the body of evidence pertaining to the consumption of food or drinks at bedtime or specifically food and drinks containing free sugars and risk of caries was rated as 'very low'. The results suggest that restricting free sugars before and at bedtime may reduce the risk of caries but studies with improved design are needed to confirm this.

Knowledge Transfer Statement: This is the first systematic review of the evidence assessing the association between caries risk in children and the consumption of food or drinks at bedtime; and

specifically foods and drinks containing free sugars at bedtime. Although the data showed a consistent positive association, the quality of evidence was very low. This means that the current recommendation to restrict food and drinks containing free sugars before bedtime in children, whilst based on a sound physiological premise, is only supported by very low quality published evidence as measured by GRADE guidelines.

Keywords: Food and drink, Cariogenic diet, dental decay, Sucrose, Schoolchildren, Night Snacks

Introduction

Dental caries is the most common global disease affecting children (Marcenes et al. 2013; Marshall et al. 2003). The caries process involves the interaction between acid-producing bacteria, sugars, and host factors including teeth and saliva over time (Selwitz et al. 2007). Free sugars are monosaccharides and disaccharides that manufacturer, cook or consumers add to food and drinks and plus the sugars naturally found in honey, syrups, fruit juices and fruit juice concentrates (World Health Organization 2015). The WHO guidelines on sugars intake for adults and children recommend that the intake of free sugars by individuals should be no more than 10% of a their total energy intake with a conditional recommendation to limit this to less than five percent (World Health Organization 2015). The Scientific Advisory Committee on Nutrition (SACN) also recommended restricting daily free sugars intake of the population to an average of no more than five percent of the total dietary intake (The Scientific Advisory Committee on Nutrition 2015). While the totality of evidence provides a basis for limiting the amount of free sugars consumed in the diet, few studies have explored the relationship between caries and patterns of eating free sugars throughout the day (Moynihan and Petersen 2004; The Scientific Advisory Committee on Nutrition 2015).

Food and drink consumed around bedtime as a caries risk factor has not been explored through systematic review. Consuming food and drinks containing free sugars around bedtime could be an important risk factor because salivary flow decreases markedly during sleep, reducing the self-

cleansing effect and the buffering capacity of saliva in the oral cavity (Weber-Gasparoni et al. 2007). This reduced nocturnal salivary flow shifts the balance toward demineralization rather than remineralization (Nauntofte et al. 2003). Evidence based clinical guidelines recommend twice daily tooth brushing with a fluoridated toothpaste; with one of the occasions being before bedtime (Duckworth and Moore 2001; Marinho et al. 2003). Therefore, it is important that studies that assess the association between caries and bedtime eating and drinking control for fluoride exposure particularly at bedtime as an important confounder. Another important factor to consider is the total amount of free sugars consumed during the day because bedtime free sugars consumption could be a proxy measure of children's high total daily free sugars intake.

This systematic review addressed three separate questions: (1) does food or drink consumption at bedtime increase the risk of dental caries in children? (2) does consuming foods containing free sugars at bedtime increase the risk of dental caries in children? and; (3) does consuming drinks containing free sugars at bedtime increase the risk of dental caries in children?

Materials and Methods

Protocol and registration

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2015). The protocol was registered in the National Institute of Health Research Database (http://www.crd.york.ac.uk/PROSPERO, Protocol I.D.CRD42016033744).

Eligibility criteria

Studies included in this review were selected following PICOS elements (reviews and dissemination 2009):

Participants: healthy children aged three-16 years old. This age period coincides with the time of greatest caries risk for children (Mejàre et al. 2014).

Intervention/exposure: The exposure was any food and drink consumption around bedtime or before sleep and specifically consuming food or drinks containing free sugars around bedtime. Specific time limits relating to the length of time that children had to eat or drink prior to bedtime were not set. However, studies had to make specific reference to food and drink consumption related to bedtime or sleeping.

Comparison: with a control group not exposed to food or drink around bedtime or without a comparison group.

Outcomes: The outcome was dental caries or early childhood caries assessed through a clinical examination. Studies reported caries prevalence, incidence, severity, measured as DMFT, dmft, DMFS, dmfs, DFS, deft, or as comparisons between caries or no caries or higher caries and lower caries groups.

Study design: Randomized controlled trials (RCTs), non-RCTs, prospective and retrospective cohort studies, case control studies and cross-sectional studies were considered for inclusion.

The excluded studies did not include children aged three-16 years or were studies that assessed nocturnal breastfeeding, or nocturnal bottle-feeding with infant formula milk. Studies that assessed

medicines containing sugars and therapeutic diets provided to children with health problems or medical conditions (other than diabetes mellitus) were also excluded.

Information Sources and Search Strategy

A comprehensive search identified relevant studies using five electronic databases (PubMed, Ovid Medline, EMBASE, Web of science and Scopus). There was no restriction placed on the time of publication (up to the 10 May 2017); the search was limited to English language articles. A Google Scholar and reference search and a hand search of reference lists from identified publications and previously published related systematic reviews was also carried out to identify any other relevant published work and other potential studies eligible for inclusion. The search strategy is shown in Appendix 1**.**

Study Selection and Data Extraction

Two reviewers (KB, SWP) independently assessed the titles and abstracts of all identified studies. The authors also obtained and independently assessed the full articles of the studies that potentially met the inclusion criteria but lacked information in the title and abstract. A third reviewer (VM) resolved any disagreements between the two reviewers.

The following information was extracted into data extraction forms: study setting, study population, inclusion/exclusion criteria, baseline characteristics, details of the exposure, study methodology, recruitment, study completion rate, dental caries outcomes and information relating to study quality.

Quality Assessment

The included studies were independently assessed by the two reviewers using the Agency for Healthcare Research and Quality (AHRQ) system (Owens et al. 2010). The AHRQ assesses eight domains: study question, study population, comparability of subjects, outcome measurement, statistical analysis, results, discussion and funding. The quality of the studies was rated as good, fair, or poor (Helfand M 2009).

For each review question, studies were organised by the study design (i.e., cohort or cross-sectional) to enable data synthesis by the 'best available evidence' synthesis (Petticrew and Roberts 2006). The quality of the body of the best available evidence for each research question was then evaluated using the GRADE Working Group guidelines (GRADE Working Group and Oxman 2004). The GRADE system rates the overall quality of evidence based on design limitations, consistency of the results across the available studies, the precision of the results, directness, likelihood of publication and risk basis using GRADE software (https://gradepro.org/). The GRADE profile analysis categorised the quality of the body of evidence as high, moderate, low, or very low. Limitations in the study quality, inconsistency of results, uncertainty about the directness of evidence and the presence of plausible residual confounding lowered the quality grade of the evidence. The footnotes related to these limitations are included in the GRADE tables in the results.

Results

Study selection

The five electronic databases identified 1267 articles; three additional studies were identified from references lists. After removing duplicate articles, 777 articles were included in the screening stage. One-hundred and thirty-eight articles were included after title screening to proceed to abstract screening. Seventy-two articles were then included for full text reading. Reviewers retrieved and independently assessed the full text articles of eligible studies with any disagreements resolved by discussion with the third review author (VM). The inter-observer agreement between the two examiners selecting the articles calculated a Kappa score of 0.85 indicating almost perfect agreement. Eighteen papers fulfilled the inclusion criteria and were included in the analysis (Figure 1). Excluded studies and the reason for exclusion are provided in Appendix 2.

Study characteristics

Table 1 summarizes the characteristics of the included studies. Studies were classified according to three age groups: 3-5 year old children, 6-11 year old children and 12-16 year old children. Four of the

18 studies were cohort studies (Gao et al. 2010; Lee and Messer 2010; Levine et al. 2007; Rugg-Gunn et al. 1984). One study was a case-control study (Palmer et al. 2010) and 13 studies were cross-sectional studies (Declerck et al. 2008; Goodwin et al. 2017; Hashim et al. 2009; Hoffmeister et al. 2016; Huew et al. 2012; Lakhanpal et al. 2014; Levine 2001; Li et al. 2011; Lueangpiansamut et al. 2012; Palacios et al. 2016; Palmer 1971; Sayegh et al. 2002; Skeie et al. 2006). Appendix 3 provides the full list of references. Eight studies assessed caries in primary teeth (Declerck et al. 2008; Gao et al. 2010; Hashim et al. 2009; Hoffmeister et al. 2016; Li et al. 2011; Palmer et al. 2010; Sayegh et al. 2002; Skeie et al. 2006). Seven papers investigated caries in permanent teeth (Goodwin et al. 2017; Huew et al. 2012; Lakhanpal et al. 2014; Lueangpiansamut et al. 2012; Palacios et al. 2016; Palmer 1971; Rugg-Gunn et al. 1984). Three papers assessed caries in both primary and permanent teeth (Lee and Messer 2010; Levine 2001; Levine et al. 2007).

Quality Assessment of individual studies

Based on the AHRQ criteria, six of the 18 studies were rated as providing good quality evidence; eight were rated as fair and four were categorised as of poor quality (see Appendix 4). A meta-analysis to address any of the three review questions was not feasible because of the inability to pool the data from cross-sectional studies due to the variability in the caries outcomes (i.e., DMFS, dmfs, DMFT, dmft, caries and fissure caries increment) and the different ways that the outcomes were presented (*i.e.* mean caries index, odds ratios, caries prevalence and number of children with caries experience). There were also variations in the follow-up periods and the type of the exposures at bedtime, specifically related to if the exposure contained free sugars. For all three research questions, it was not possible to produce a risk of bias funnel plot because only four longitudinal studies were included in the systematic review.

Quality assessment of the body of evidence using GRADE

As part of the GRADE process, the consistency of the associations across the study types was reviewed for the three different age groups (Table 1). For children aged 3-5 years, all seven studies (one cohort, five cross-sectional and one case-control) showed a consistent positive association between bedtime food or drink and dental caries. For children aged 6-11 years, both cohort studies and four of the five cross-sectional studies showed a positive significant association. One study showed a non-significant association. For children aged 12-16 years, one cohort study and two out of the four cross-sectional studies reported a positive significant association. The remaining two cross-sectional studies showed a non-significant association.

The GRADE assessment for each research question was based on cohort studies in the absence of randomized clinical trials (RCTs), and cross-sectional studies in the absence of RCTs. Three GRADE Profile tables were produced related to each review question (see Appendix 5).

Does consuming food or drinks at bedtime increase the risk of dental caries?

Four cross-sectional studies provided the best available evidence on the effect of consuming foods or drinks at bedtime and on caries risk (Table 2). Three studies investigated primary teeth and one study assessed children with permanent teeth. The studies were consistent with three of the four studies showing a statistically significant association between food or drinks at bedtime and the risk of dental caries (Declerck et al. 2008; Li et al. 2011; Palmer 1971). Two cross-sectional studies assessed the consumption of food and drinks at bedtime without specifying if the food or drinks contained free sugars. Neither study reported food and drinks separately (Hashim et al. 2009; Palmer 1971) (Table 2). Overall, the quality of evidence for assessing the association between food and drinks consumed at bedtime and caries in children was 'very low' (see Appendix 5; Table 5: S1). The reason for the quality downgrade was related to the plausible confounding that would reduce the effect. The studies did not control for confounding factors such as brushing before bedtime, fluoride exposure and daily intake of free sugars.

Does consuming foods containing free sugars at bedtime increase the risk of dental caries in children?

Three cohort studies investigated the causal relationship between consuming food containing free sugars at bedtime and were used for the GRADE profile analysis (Appendix 5, Table 5: S2). Two cohort studies included children with permanent teeth and one study in children with primary teeth. The cohort studies were consistent in showing higher caries levels in children specifically exposed to food containing free sugars at bedtime (Table 3) (Gao et al. 2010; Levine et al. 2007; Rugg-Gunn et al. 1984). The quality of the evidence was downgraded to very low because of the plausible confounding. Two of the three cohort studies did not control for the total amount of free sugars consumed during the day. All cohort studies controlled for tooth brushing and fluoride; however, none of them assessed bedtime tooth brushing.

Consistent with the GRADE analysis of the cohort studies, analysis of three cross-sectional studies showed a positive statistical association between bedtime exposure to food containing free sugars and dental caries in children (Table 1). One cross-sectional study specifically assessed the association between sweets and the consumption of snacks containing free sugars and caries in permanent teeth (Lueangpiansamut et al. 2012), while one study assessed consumption of confectionery at bedtime in primary teeth (Sayegh et al. 2002). The third study assessed caries in both primary and permanent teeth (Levine 2001). These cross-sectional studies also found an increased risk of dental caries in children consuming snacks containing free sugars at bedtime (Levine 2001; Lueangpiansamut et al. 2012; Sayegh et al. 2002).

Does consuming drinks containing free sugars at bedtime increase the risk of dental caries in children?

Two cohort studies were used for the GRADE profile analysis relating to the risk of dental caries and consumption of drinks containing free sugars at bedtime (Appendix 5; Table 5: S3) (Lee and Messer 2010; Levine et al. 2007). Both cohort studies assessed dental caries in children with permanent teeth and reported drinks containing free sugars separately to foods containing free sugars. The studies showed a consistent statistically significant positive association between risk of dental caries and consumption of drinks containing free sugars at bedtime. The GRADE profile analysis classified the evidence as very low quality (Supplemental material 5, Table 5: S3).

Data from cross-sectional studies were consistent with the cohort studies. In the primary dentition, four of the five cross-sectional studies found a highly statistically significant association between consuming drinks containing free sugars at bedtime and dental caries (Declerck et al. 2008; Hoffmeister et al. 2016; Levine 2001; Skeie et al. 2006). For the permanent dentition, one cross-sectional study showed a statistically significant association between drinks containing free sugars at bedtime and the mean DMFT of children aged 6 to 11 years (Levine 2001).

Although the three cross-sectional studies assessed food and drinks containing free sugars and caries in permanent teeth, they did not report data for drinks separately to that for foods. Two studies showed a significant positive association between consuming food or drinks containing free sugars and dental caries in children (Goodwin et al. 2017; Lakhanpal et al. 2014).

Discussion

This systematic review assessed the evidence related to the caries experience of children aged 3-16 years of age and consuming any food or drinks and consuming food and drinks containing free sugars at bed time. Eighteen papers were identified that fulfilled the inclusion, which were all observational studies (i.e. no RCTs). The studies were categorized into three age groups to recognise the different

eating and drinking habits that children have across their life course. This systematic review provided most consistent evidence for the relationship between bedtime exposures to free sugars and caries in younger children with all seven studies on preschool children age (3-5 year old) reporting statistically significant positive associations.

Despite the studies showing consistent positive associations, the quality of body of evidence related to all three research questions was classified as 'very low'. The main reasons for this related to the type of study (observational) and the failure to control for plausible confounders. For example, two cohort studies assessed drinks containing free sugars at bedtime; however, neither study controlled for the total daily free sugars intake by children and for this reason, the evidence was downgraded (risk of plausible confounding). **Study design**

The GRADE criteria for evaluating the strength of the body of evidence recognizes (in the absence of RCTs) the importance of assessing evidence from studies using other study designs. However, observational studies provide lower quality evidence and all 18 studies included in this systematic review were observational studies, and as such initially classified as 'low' quality evidence (GRADE Working Group and Oxman 2004). Caution should always be applied when relying on cross-sectional studies to assess the relationship between diet and dental caries because one cannot establish a temporal relationship between exposure and outcome. Assessment for the risk of bias using funnel plots was not possible and therefore the presence of publication bias cannot be excluded, however data were not downgraded for this factor. A further limitation of this systematic review is that it included English language papers only, which may have increased the risk of publication bias.

Lack of controlling for confounders

Eight of the included studies investigated tooth brushing frequency in children (Declerck et al. 2008; Gao et al. 2011; Lakhanpal et al. 2014; Lee and Messer 2010; Levine et al. 2007; Li et al. 2011; Palacios et al. 2016; Sayegh et al. 2002). Four studies assessed other tooth brushing related factors such as age of starting tooth brushing (Hoffmeister et al. 2016; Li et al. 2011; Sayegh et al. 2002; Skeie et al. 2006),

types of toothpaste (Lee and Messer 2010; Rugg-Gunn et al. 1984; Sayegh et al. 2002) and parental supervision of tooth brushing (Hoffmeister et al. 2016; Skeie et al. 2006). However, only two studies specified the timing of tooth brushing as before bedtime or in the evening (Li et al. 2011; Lueangpiansamut et al. 2012).

Most of the included studies did not control for the daily amount of free sugars consumed by children. Rugg-Gunn *et al.* (1984) controlled for the daily amount of total sugars consumed and the bedtime exposure and showed that the relationship between bedtime free sugars and caries was not significant after controlling for total daily free sugars intake. However, Goodwin *et al*. (2017) controlled for the total amount of free sugars consumed in the day and found that free sugars consumed at night was possibly a more important determinant of caries experience than free sugars snacks during the day (Goodwin et al. 2017). The percentage of energy from free sugars was not significantly different in those children who consumed free sugars in the hour before bed and those who did not (19.8% vs. 18.8%), indicating that bed time sugars was not simply a proxy for overall free sugars consumption (Goodwin et al 2017). This systematic review underscores the importance of primary studies assessing fluoride exposure specifically at bedtime and the daily free sugars intake to exclude these important confounders.

Variations in the measurement of bedtime exposure

The definition of bedtime sugars intake varied between the studies. Two studies by Levine et al, used a dietary questionnaire and defined bedtime consumption as one hour before bed (Levine 2001; Levine et al. 2007). In contrast, Plamer (1971) defined bedtime as in bed or within 15 minutes of the child going to bed. Rugg-Gunn *et al.* (1984) measured the length of time between food/drink intake, categorized according to its free sugars content, and bedtime. The other studies defined bedtime without specifying the time before sleep using more vague questions involving eating or drinking before bedtime (Hashim et al.), bedtime eating (Li et al. 2011), drinks at bedtime (Hoffmeister et al. 2016; Skeie et al. 2006), drinks at night or snacks at night containing free sugars (Declerck et al. 2008),

eating sweets before bedtime (Gao et al. 2010; Lueangpiansamut et al. 2012) and confectionery eaten at bed or night time (Sayegh et al. 2002). The variation identified in this review suggests that future studies should adopt a standard definition or reach a consensus about what is meant by bedtime exposure to allow comparison between studies.

Clinical implications: existing guidelines that make recommendations about bedtime food and drink intake

Several clinical guidelines have made recommendations about patterns of eating, which have not been based on systematic review or robust analysis of the best available evidence. The National Health Service (NHS) Scotland guideline recommends avoiding foods and drinks containing free sugars at bedtime (NHS Health Scotland 2012). This guideline cites supporting evidence from three previously published guidelines and from one professional society lecture paper (Committee on Medical Aspects of Food Policy 1989; Levine and Stillman-Lowe 2009; Moynihan 2005; World Health Organization 2003). The Public Health England "Delivering Better Oral Health" evidence-based toolkit recommends not eating or drinking in the last hour before bed (Public Health England 2014). This recommendation cites a cross-sectional study that includes a comparison of 600 children in North England (Levine 2001). The American Academy of Pediatric Dentistry (AAPD) recommends limiting the provision of drinks and snacks containing free sugars to children at night to reduce the risk of caries in children (The American Academy of Pediatric Dentistry 2017). The Ministry of Health in Australia guidelines recommend children do not have food and drinks at bedtime (The Ministry of Health 2014). The European Academy of Paediatric Dentistry guidelines on prevention of early childhood caries discourages the frequent intake of sweet drinks, especially at night-time (The European Academy of Paediatric Dentistry guidelines 2008). In the UK, the "Scientific Basis of Oral Education" recommends avoiding drinks or snacks containing free sugars at bedtime (Levine and Stillman-Lowe 2014), the authors state that the

recommendation supported by the majority of relevant research studies, however, they only cite one reference to support this statement (Levine 2001).

This current evidence synthesis provides an objective and more robust analysis of the totality of the evidence relating to children aged 3-16 years. Using the current analysis to set recommendations through the GRADE process (GRADE Working Group and Oxman 2004) would require evaluation of factors including the balance of desirable and undesirable effects, value and preferences and use of resources to implement recommendations – which was beyond the scope of the current work. In setting formal recommendations, it would be important to consider any undesirable effects of limiting bedtime dietary intake such as risk of undernutrition, because bedtime intakes may make an important contribution to overall energy intake. However, only limiting foods and drinks that contain free sugars is likely to reduce overall free sugars intake, which would have a desirable impact on health.

Research requirements

This systematic review has identified that there are no RCTs and few cohort studies investigating whether bedtime food and drink at bedtime increases risk of dental caries in children aged 3-16 years. The limited and very low quality evidence highlights the need for more well-designed primary research exploring the relationship between food and drink consumption, especially food and drinks that contain free sugars at bedtime and the risk of dental caries. Future studies should consider adopting a standard definition of bedtime exposure to free sugars and ensure that studies adequately control for the daily amount of free sugars and fluoride exposure at bedtime as key confounders.

Conclusion

The outcome of this systematic review provides consistent, albeit very low quality evidence, to support current recommendations to limit consumption of foods and drinks containing free sugars at

bedtime for children aged 3-16 years. This evidence was more consistent for preschool age children than older age groups.

Author Contributions

Baghlaf K, contributed to the conception, protocol, design, literature search, screening of the relevant studies, data extraction, AHRQ assessment, analysis, GRADE tables, interpretation and critically revised the manuscript; Muirhead V contributed to conception, protocol, design, screening of the relevant studies, data extraction, analysis, GRADE tables, interpretation and critically revised the manuscript; Moynihan P contributed to conception, protocol, design, analysis, AHRQ assessment, GRADE tables, interpretation and critically revised the manuscript; Weston Price S contributed to the literature search, screening the relevant studies, data extraction, AHRQ assessment conception, data analysis, interpretation and critically revised the manuscript; Pine C contributed to conception, design, data interpretation, GRADE tables and critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

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Figure/table legend

Figure. A PRISMA flow diagram showing the number of articles identified at each stage of the search

Table 1. Summary of included studies: characteristics and exposure/outcome relationship

Table 2. Summary of cross-sectional studies used in the GRADE assessment

Table 3. Summary of cohort studies used in the GRADE assessment